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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,093	05/10/2001	Preeti G. Lal	PF-0357-1 DIV	8489

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,093	LAL ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,15-20 and 35-37* is/are pending in the application.

4a) Of the above claim(s) *5-10,15-20 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☒ Claim(s) *2, 4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Sitton.

2. Currently, claims 1-10, 15-20 and 35-37 are pending in the instant application. Claims 5-10, 15-20 and 35-37 are withdrawn from consideration as drawn to non-elected invention. The amendments and arguments have been thoroughly reviewed but are insufficient to place the instant application in condition for allowance. The following rejections are maintained. They represent the complete set being applied in the instant application. Response to arguments follows. This action is FINAL.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

WITHDRAWN REJECTIONS

4. The rejection of claim 2 made in the previous office action (lack of written description, page 3) under 35 USC 112/first paragraph is withdrawn in view of the amendment to claims 2.

5. The rejection of claims 1-4 under 35 USC 112/first paragraph (lack of enablement) made on page 7 of the previous office action is withdrawn in view of the amendment to claim 1 to delete "biologically active fragment" and in claim 3 to delete the recitation of "effective amount".

6. The rejection of claims 3 and 4 under 35 USC 112/2nd paragraph made on page 9 of the previous office action is withdrawn in view of the amendment to claim 3 to delete "effective amount".

7. The rejections of claim 2 made under 35 USC 102(b) on page 10 of the previous office action are withdrawn in view of the amendment to claim 2.

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 112

8. Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is maintained and reiterated as set forth on pages 3-7 of the previous office action.

Response to Arguments

9. The response traverses the rejection. The response asserts that claim 1 has been amended and no longer encompasses 'any' amino sequence within SEQ ID NO: 1. This argument was thoroughly reviewed but was not found persuasive because the claims remain directed to "an isolated polypeptide 'comprising' *an* amino acid sequence of SEQ ID NO: 1" (preamble and section a of claim 1). The claims do not set forth which specific amino acid sequence from within SEQ ID NO: 1 are being claimed, and the broad recitation of "an amino acid sequence of" reads on any fragment from within SEQ ID NO: 1 with no minimum length limitation.

The response further asserts that the claims meet the written description requirement as set forth by the guidelines in the MPEP. The response asserts that SEQ ID NO: 1 has been disclosed by the specification and that the specification teaches preferred variants of SEQ ID

NO: 1 include proteins with 80%, 90%, and 95% identity to SEQ ID NO: 1. This argument has been thoroughly reviewed but was not found persuasive. The specification passages cited by the response refer to variants which are contemplated by the specification. The specification does not actually teach any specific variants. The variants encompassed by the claims include both variants with the same or similar biological or functional activity as well as functional mutants. The chemical and structural features taught at page 12, lines 1-20 are potential domains and bonding sites and do not teach how the peptide of SEQ ID NO: 1 can be altered to either retain or alter it's activity. The teachings in the specification do not represent species of the broadly claimed genus of 'variants'. The response asserts that both the Fiers v. Revel and Lilly citations are drawn to case law where the claims in question possessed only functional attributes with no structural features and that in the instant case, the claims possess structure. This argument has been thoroughly reviewed but was not found persuasive as the claims in question represent only partial structures. No structure/function correlation has been provided by either the specification or the claims to determine which amino acids within SEQ ID NO: 1 can be mutated to either retain or alter the biological activity or function of SEQ ID NO: 1. The WRITTEN DESCRIPTION guidelines which applicant cites specifically refer to "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure". As stated earlier, no structure/function correlation has been disclosed in either the specification or the claims with regard to the large genus of variants (encompassed by both sections a and b of claim 1). It is further noted that with regard to section c, the claims still encompass a minimum of 15 consecutive amino acids of SEQ ID NO: 1 with any amino acid sequence on either side due to

the preamble recitation of 'comprising'. Such recitation, along with section a, represent an even larger genus of variants of SEQ ID NO: 1 than section b. Altogether, the claims are drawn to a large genus of variants, mutants, and homologs of SEQ ID NO: 1 for which the disclosure of the single polypeptide sequence of SEQ ID NO: 1 is not representative.

The response further references Brenner et al in teaching that "30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues", and that 40% or more identity over at least 70 residues is reliable in signifying homology between proteins. This argument has been thoroughly reviewed but was not found persuasive as the recitation of Brenner does not limit the scope of the claimed invention. The claims continue to encompass variants, mutants and homologs of SEQ ID NO: 1 which have not been taught or described in the specification. Additionally, with regard to the teachings of Brenner, Fetrow teaches (Fetrow et al., J. Mol. Biol., vol. 282, pp 703-711, 1998) that although function prediction by homology to previously characterized proteins is extremely successful and is fast, cheap and reliable, there are several problems that limit its potential utility, one of which is that sequence homology does not guarantee functional similarity (p 704, col. 1, 1st full paragraph). Fetrow teaches that "threading"(analysis using structure prediction tools) can identify topological cousins, that is , protein families such as the α/β barrels with similar structures, but dissimilar functions. Fetrow teaches using a three dimensional descriptor of the active site of a protein, termed "fuzzy functional form" (FFF) and argues that threading alone is not enough to provide the required information about function because it has been shown that pairs of proteins can have similar structures but unrelated functions (p. 706, col. 2, last para). Fetrow teaches that because such topological cousins exist, knowledge of the structure is not

equivalent to identification of protein function. Skolnick (Skolnick and Fetrow, TIBTECH, January 2000, vol. 18, pp 34-39) teaches (p. 35, "Box 1") that a common protein characteristic that makes functional analysis based only on homology especially difficult is the tendency of proteins to be multifunctional. Skolnick teaches that for example, lactate dehydrogenase binds NAD, substrate, and zinc and performs a redox reaction and that each of these occurs at different functional sites that are in close proximity and the combination of all four sites creates the fully functional proteins. Skolnick also cites RecA which contains a DNA binding domain, a multimerization domain and additional sites that bind regulatory proteins. Skolnick also teaches that the serine threonine phosphatase superfamily is a prime example of the difficulties of using standard sequence analysis to recognize the multiple functions found in single proteins. Skolnick teaches that this large protein family is divided into a number of subfamilies, all of which contain an essential phosphatase active site. He teaches that subfamilies 1, 2A and 2b exhibit 40% or more sequence identity between them, however each of these subfamilies is apparently regulated differently by the cell and observation suggest that there are different functional sites at which regulation can occur. Skolnick teaches that because the sequence identity between subfamilies is so high, standard sequence similarity methods could easily misclassify new sequences as members of the wrong subfamily if the functional sites are not carefully considered. The art specifically teaches, that sequence alignment alone does not necessarily provide a predictable correlation between the structure and specific function of a protein. For these reasons and the reasons made of record in the previous office action, the rejection is maintained.

Claim Rejections - 35 USC § 102

10. Claims 1 and 3 are rejected under 35 USC 102(b) as being anticipated by the 1993 Sigma Chemical Catalogue product P 2254.

The rejection is maintained and reiterated as set forth on page 10 of the previous office action.

11. Claims 1 and 3 are rejected under 35 USC 102(b) as being anticipated by Mochizuki et al (US Patent 5,395,916; March 1995).

The rejection is maintained and reiterated as set forth on page 10 of the previous office action.

Response to Arguments

12. The response traverses both 102(b) rejections. The response asserts that none of the cited references teach SEQ ID NO: 1, a variant of SEQ ID NO: 1 having at least 95% sequence identity to SEQ ID NO: 1, or a fragment of SEQ ID NO: 1 having at least 15 contiguous residues of SEQ ID NO: 1. This argument has been thoroughly reviewed but was not found persuasive as the claims remain directed to "an isolated polypeptide 'comprising' *an* amino acid sequence of SEQ ID NO: 1" (preamble and section a of claim 1). The references teach 'an' amino sequence of SEQ ID NO: 1, and therefore anticipate the claims (claim 3 is dependent from claim 1, and both reference teach a 'composition'). The claims do not set forth which specific amino acid sequence from within SEQ ID NO: 1 are being claimed, and the broad recitation of "an amino acid sequence of" reads on any fragment from within SEQ ID NO: 1 with no minimum length limitation. Therefore, the rejections are maintained.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Claims 2 and 4 are objected for being dependent on rejected claims. Claims 1 and 3 are rejected. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Jehanne Sitton
Primary Examiner
Art Unit 1634

Jehanne Sitton
5/17/04